DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Atlanta District Office
NC-35 481

60 8th Street, N.E.
Atlanta, Georgia 30309

October 15, 1997

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Teresa B. Phykitt
President
Health Corporation
620 Health Drive
Rocky Mount, North Carolina 27804

WARNING LETTER

Dear Ms. Phykitt:

An inspection of your drug manufacturing facility was conducted on September 22-30, 1997, by Investigator Kathleen D. Culver. Our investigator documented several significant deviations from the Current Good Manufacturing Practice Regulations (GMPs) as set forth in Title 21 of the Code of Federal Regulations (21 CFR), Part 211. These deviations cause your drug product, Aquaprin, to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

You failed to conduct an appropriate assessment of each batch of drug product for conformance to final specifications for the drug product prior to release. Your quality control unit failed to perform an adequate review of drug product production and control records to determine compliance with all established, approved specifications before the batch was released for distribution. This review should have included a thorough investigation of any unexplained discrepancies or the failure of a batch to meet any of its specifications.

You have failed to appropriately investigate and respond to out of specification (OOS) results. You have failed to maintain adequate documentation to substantiate the invalidation of OOS results obtained during content uniformity and assay testing on finished product. No investigation was performed of OOS results for several lots. When investigations were conducted, entries such as "more than likely", "may", and "undetermined problem" were noted in the investigational records. The assumptions made as to the reason for the OOS results were speculative at best, based on the supporting documentation available. We are concerned that your OOS investigation methodology and the conclusions made have concealed true product quality problems.

Lot 6005 had an initial lot composite assay which failed specifications. Retesting performed on another composite sample was the basis for release of the lot. No investigation was performed of these failing results.

Lot 7002 had initial low assay results in two of six sample results. The lot was released based on the averaging of the six available assay results. No investigation was performed of these failing results.

The composite sample for Lot 5006 failed the content uniformity testing after Level 1 and Level 2 testing. The lot was subsequently released based upon passing content uniformity results obtained from other samples analyzed as part of a filling validation study. A notation was made by quality control that the content uniformity results cited for lot release were the average of the validation content uniformity results. There was no investigation of the failing results.

Lot 5007 failed the initial content uniformity testing. Level 1 and Level 2 testing performed later by another analyst also failed. Retesting performed by a third analyst yielded acceptable results which were the basis for lot release. A Release Justification Report issued for this lot referenced the findings of a failure investigation into Lot 6001. The conclusion made was that "some unknown (at this time) problem occurred with the analytical testing". There is no conclusive evidence to support the contention made in this report. In fact, the method validation study using the USP test methods for assay and content uniformity indicated that the methods were suitable for use with this product formulation.

A composite sample for Lot 6001 failed initial content uniformity at Level 1 and Level 2 testing. The lot was then divided into "sublots" in an attempt to release portions of the lot which met content uniformity criteria on retest. Three of these sublots failed content uniformity testing. A third sampling of ten units from the lot composite sample was tested later and found acceptable. The lot was released based on the last results obtained.

The 3 month ambient stability assay sample for Lot 5004 revealed one of three samples to yield a failing assay result. No investigation was conducted into this result and it was averaged with the other passing results prior to reporting.

You have failed to ensure that each person engaged in the manufacture, processing, and packaging of this drug product, and each person responsible for supervising these activities, has the education, training, and experience to enable that person to perform their assigned functions in such a manner as to provide assurance that your drug product has the quality and purity that it purports or is represented to possess. This lack of training was exemplified by the handling of the above OOS results. You informed our investigator that you have little knowledge of manufacturing processes and GMP issues.

You have failed to maintain an ongoing stability testing program to ensure that your product meets applicable standards of identity, strength, quality, and purity throughout its labeled expiration date. You failed to test the 9 month or 12 month ambient stability samples for Lot 6002 (the annual stability lot for 1996). You failed to test the 3 month or 6 month ambient stability sample for Lot 7001 (the annual stability lot for 1997). Your analytical laboratory has

not been staffed since March 1997 and you have made no arrangement to have the appropriate testing performed by a contract laboratory. However, your products remain on the market and you continue to ship from available stock at your facility.

The process validation study of the filling process on line two was reported to be successful although seven average fill weights did not meet the acceptance criteria in the protocol. These OOS fill weights were not evaluated or explained in the summary validation report. This report was reviewed and approved by five responsible individuals at your firm. Similarly the validation of Line 1 was also judged to be successful although high and low fill weights were observed in Lot 6001.

Many of the above deviations were included on the FDA 483 (Inspectional Observations) which was issued to and discussed with you at the conclusion of the inspection. The violations noted in this letter and in the FDA 483 are symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. The deviations discussed above and included on the FDA 483 should not be construed as an all inclusive list of violations which may be in existence at your firm. It is your responsibility to ensure adherence to each requirement of the Act. We are submitting your product labeling to the Center for Drug Evaluation and Research for their review. You may receive further correspondence from FDA if labeling discrepancies are found.

You are responsible for investigating and determining the causes of the violations identified by FDA. You should take immediate actions to correct these violations. Failure to promptly correct these deviations may result in legal sanctions provided by the law such as product seizure and/or injunction, without further notice to you. Federal agencies are advised of the issuance of all warning letters involving drugs so that they may take this information into account when considering the award of contracts.

You should notify this office in writing, within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which corrections will be completed. We are cognizant of the fact that you are currently not manufacturing product. We are concerned however that you continue to fill orders and distribute product from lots discussed above. Your response should address any proposed actions regarding products currently in distribution which have not been properly tested. Your response should be addressed to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead.

Sincerely,

Ballard H. Graham, Director
Atlanta District